UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/121,211	07/23/98	SHINOHARA T	B0801/7116

HM12/0813

EDWARD R. GATES
WOLF, GREENFIELD & SACKS
600 ATLANTIC AVENUE
BOSTON MA 02210

EXAMINER	
ROMEO, D	

ART UNIT	PAPER NUMBER
1647	20

DATE MAILED: 08/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

Office Action Summary	Application No. 09/121,211	Applicant(s) Shinohara et al.
	Examiner David Romeo	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *29 May 2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22, 26, 29, 31, 34, 35, 44, 45, 47, 49, 52, 55, 56, 58, 61, 64,* 70 is/are pending in the application.

4a) Of the above, claim(s) *12-22, 29, 31, 34, 35, 44, 45, 47, 49, 52, 55, 56,* 58,61,64,70 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4-11, and 26* is/are rejected.

7) ☒ Claim(s) *2 and 3* is/are objected to.

8) ☒ Claims *1-22, 26, 29, 31, 34, 35, 44, 45, 47, 49, 52, 55, 56,* 58,61,64,70 are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/29/2001 (Paper No. 16) has been entered.

2. Claims 1-22, 26, 29, 31, 34, 35, 44, 45, 47, 49, 52, 55, 56, 58, 61, 64, 70 are pending. Claims 12-22, 29, 31, 34, 35, 44, 45, 47, 49, 52, 55, 56, 58, 61, 64, 70 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 9. Claims 1-11, 26 are being examined. Claim 26 is being examined only to the extent that it reads upon an agent that is a nucleic acid molecule. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 8, 10, 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO:1 which corresponds to a nucleic acid sequence encoding the human species of the LEDGF protein comprising the amino acid sequence of SEQ ID NO:2. LEDGF stimulated the growth of lens epithelial cells (Example 6). COS cells over-expressing LEDGF attached themselves to the bottom of culture plates much faster than cells containing only vector (Example 7). The claims are directed to or encompass any and all nucleic acid molecules that hybridize to SEQ ID NO: 1 and encode a protein that stimulates the synthesis of any and all proteins in any and all epithelial cells. There is no description of such hybridizing nucleic acid molecules or of the proteins they encode having the desired activity. With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and therefore conception is achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Whereas the instant specification provides a detailed description of a particular DNA molecule, SEQ ID NO:1, encoding a particular protein, SEQ ID NO:2, the instant specification does not provide a structural formula which is definitive of all hybridizing DNA molecules and mutated variants thereof that encode a protein with the desired activity. Nor has the specification described any and all nucleic acid agents that "selectively bind" to any and all nucleic acid molecules that hybridize to SEQ ID NO: 1 and encode a protein with the desired activity. Applicants' arguments

have been fully considered but they are not persuasive. Example 9 of the revised interim written description guidelines training materials is clearly distinguishable from the instant application because example 9 is directed to a situation wherein the specification disclosed a single cDNA (SEQ ID NO:1) which encoded a protein that bound to a dopamine receptor and stimulated adenylate cyclase activity. The specification included an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of cDNAs that encoded proteins that bound to dopamine receptor and stimulated adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1. In the instant application, unlike example 9, the specification does not include an example wherein other cDNAs that encoded proteins that stimulated the synthesis of any and all proteins in any and all epithelial cells were isolated. Furthermore, the instant specification at page 49, lines 6-8, only describes results indicating that LEDGF regulated the synthesis and accumulation of several proteins in mouse LECs, whereas the claims are directed to inducing the synthesis of any and all proteins in any and all epithelial cells, which the specification does not describe.

4. Claims 1, 8, 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1, does not reasonably provide enablement for nucleic acid molecules which hybridize to SEQ ID NO:1 and encode a polypeptide that induces protein synthesis in an epithelial cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification discloses SEQ ID NO:1 which corresponds to a nucleic acid sequence encoding the human species of the LEDGF protein comprising the amino acid sequence of SEQ ID NO:2. LEDGF stimulated the growth of lens epithelial cells (Example 6). COS cells over-expressing LEDGF attached themselves to the bottom of culture plates much faster than cells containing only vector (Example 7). The claims are directed to or encompass any and all nucleic acid molecules that hybridize to SEQ ID NO: 1 and encode a protein that stimulates the synthesis of any and all proteins in any and all epithelial cells. However, the instant specification does not identify those amino acid residues in the amino acid sequence of a LEDGF which are essential for its biological activity and structural integrity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of random insertional, deletional and substitutional mutation analysis of codons encoding over 500 amino acid residues before they

could even begin to rationally design a polynucleotide that hybridizes to SEQ ID NO: 1 and encodes a functional LEDGF having other than a natural amino acid sequence. The disclosure of a single DNA sequence encoding a single LEDGF with a natural amino acid sequence is insufficient support under 35 U.S.C. § 112, first paragraph, for claims which encompass any and all polynucleotides encoding any and all LEDGFs, including mutants thereof, which are encoded by a DNA which hybridizes to a DNA having that single disclosed sequence under the recited stringency conditions. Moreover, there is a lack of predictability in the art. Ngo (w10)[1] teach that the native structure of a protein is a unique three-dimensional structure into which the protein folds under physiological conditions and all the information necessary to determine the native structure can be contained in the primary amino acid sequence (page 433, full paragraph 1). However, it is not even known whether there exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone (page 492, full paragraph 2). Furthermore, a nucleic acid molecule that hybridizes to SEQ ID NO: 1 is antisense to SEQ ID NO: 1 and encodes polypeptides having no function identified in the specification. Such polypeptides would be entirely unrelated in structure to the LEDGF amino acid sequence described. Absent either a useful functional property or any structural (and hence functional)

---

[1]Citations by the examiner are in an alphanumeric format, such as "(a1)", wherein the "a" refers to the reference cited on the Notice of References Cited, PTO-892, and the "1" refers to the Paper No. to which the Notice of References Cited, PTO-892, is attached.

relationship to the exemplified LEDGF corresponding to the full scope of the subject matter claimed, the artisan cannot use all of the claimed materials for any purpose described in the disclosure absent undue experimentation. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

New formal matters, objections, and/or rejections:

Claim Objections

5. Claim 26 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n).

6. Claims 5, 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 16, and 18 nucleotide fragments do not further limit and do not infringe a 20 nucleotide fragment.

Claim Rejections - 35 USC § 112

7. The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 26 is indefinite because it is unclear if the kit or the package contains the nucleic acid. The metes and bounds of the claim(s) are not clearly set forth. It is suggested that the claims recite wherein the package contains.

b. Claims 1, 4 are indefinite over the recitation of "complements of" because it is unclear if a polynucleotide that is the complement, a polynucleotide that is a portion of the complement, or a polynucleotide comprising either continuous or discontinuous complements is intended. The metes and bounds of the claim(s) are not clearly set forth.

c. Claim 5 recites the limitation "the sequence group". Either there is insufficient antecedent basis for this limitation in the claim or the antecedent basis for this limitation is unclear. The metes and bounds of the claim(s) are not clearly set forth.

d. Claim 7 is indefinite over the recitation of "encodes a polypeptide, or fragment of, which binds a human antibody" because in view of the use of the indefinite article in the phrase "a polypeptide", the broadest reasonable interpretation of the claim is that it is directed to a nucleic acid molecule encoding a polypeptide corresponding to any contiguous subset of the codons within the nucleic acid molecule. It is unclear which polypeptide is intended.

e. Claim 4 is indefinite over the recitation of "complements of" SEQ ID NO: 14, 15 or 16 because SEQ ID NO: 14, 15, and 16 are amino acid sequences and the specification fails to define a complement of an amino acid sequence. One of ordinary skill in the art would not be reasonable apprised of the metes and bounds of the claimed invention. The metes and bounds of the claim(s) are not clearly set forth.

f. Claim 7 is indefinite over the recitation of "a fragment of" because the antecedent basis for this limitation is unclear. The metes and bounds of the claim(s) are not clearly set forth.

g. Claim 6 is indefinite over the recitation of "the fragment" because the antecedent basis for this limitation is unclear.

h. Claim 4 is indefinite because the phrase "fragments of (1) and (2)" is recited in an improper Markush format. The metes and bounds of the Markush group are not clearly set forth. When materials recited in a claim are so related as to constitute a proper Markush group, they may be recited in the conventional manner, or alternatively. For example, if "wherein R is a material selected from the group consisting of A, B, C and D" is a proper limitation, then "wherein R is A, B, C or D" shall also be considered proper. See M.P.E.P. 2173.05(h). It is suggested that the claims recite "fragments of (1) or (2)".

i. Claim(s) 4 is indefinite because it recites the term "unique". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "unique" an artisan cannot determine what additional limitations

are placed upon a claim by the presence of this term. The metes and bounds of the claim(s) are not clearly set forth.

j. Claim(s) 26 is indefinite because it recites the term "selectively binds". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "selectively binds" an artisan cannot determine what additional limitations are placed upon a claim by the presence of this term. The metes and bounds of the claim(s) are not clearly set forth.

k. Claim 1 is indefinite because it is unclear if the limitations in parentheses are merely exemplary of a hybridization buffer or if they are intended to limit the hybridization buffer. The metes and bounds of the claim(s) are not clearly set forth. It is suggested that the claims recite wherein the hybridization buffer comprises.

8. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid molecule encoding a polypeptide that binds a human antibody. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claim 7 specifies a nucleic acid molecule encoding a polypeptide that binds a human antibody. In view of the use of the indefinite article in the phrase "a polypeptide", the

broadest reasonable interpretation of the claim is that it is directed to a nucleic acid molecule encoding a polypeptide corresponding to any contiguous subset of the codons within the nucleic acid molecule. Furthermore, there are no structural or functional limitations to the human antibody. The claims accordingly read on polypeptides having no function identified in the specification. They additionally read on polypeptides encoded by alternate reading frames within the nucleic acid molecule. Such polypeptides would be entirely unrelated in structure to the LEDGF amino acid sequence described. Absent either a useful functional property or any structural (and hence functional) relationship to the exemplified LEDGF corresponding to the full scope of the subject matter claimed, the artisan cannot use all of the claimed materials for any purpose described in the disclosure absent undue experimentation.

9. Claims 4-7, 9, 11, 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule consisting of a fragment of SEQ ID NO: 1, wherein said fragment is between 20 and 3360 nucleotides long, does not reasonably provide enablement for an isolated nucleic acid molecule that is a fragment of SEQ ID NO: 1 between 20 and 3360 nucleotides in length which is not identical to "fragments of (1) and (2)". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. There are no limitations to the "fragments of (1) and (2)". A single nucleotide is a

fragment. SEQ ID NO: 21 includes nucleotides G, A, T, and C. The claims encompass nucleic acid molecules that are 20-3360 nucleotide fragments of SEQ ID NO: 1 but do not include G, A, T, or C. The specification lacks guidance for making, and working examples of, such nucleic acid molecules.

Specification

10. The disclosure is objected to because of the following informalities: Hyperlinks and/or other forms of browser-executable code in the text of a patent application are impermissible and require deletion. Hyperlinks and/or other forms of browser-executable code are included in the patent application. See, for example, page 12, line 19. This example is not meant to be an exhaustive list. The application cannot issue until all hyperlinks and/or other forms of browser-executable code in the text the patent application are deleted.

Appropriate correction is required.

Conclusion

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ochs (C2, cited by Applicants) teaches an isolated nucleic acid molecule that is 99.4% identical to nucleotides 848 to 3360 of SEQ ID NO: 1, which would hybridize to the complement

of SEQ ID NO: 1 under the recited conditions and encode a polypeptide that induces protein synthesis in an epithelial cell, absent evidence to the contrary.

12. Claims 2, 3 are objected to as being dependent upon a rejected base claim.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

AUGUST 12, 2001